International Workshop on Alternative Methods to Reduce, Refine, and Replace the Use of Animals in Vaccine Potency and Safety Testing: State of the Science and Future Directions

William H. Natcher Conference Center, Bethesda, MD, USA
September 14-16, 2010

Agenda

Organizers

- Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)
- National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM)
- European Centre for the Validation of Alternative Methods (ECVAM)
- Japanese Center for the Validation of Alternative Methods (JaCVAM)
- Health Canada

Abstract

Vaccines represent a vital and cost-effective tool in the prevention of numerous infectious diseases. The increasing occurrence of antibiotic-resistant bacteria, the emergence and re-emergence of zoonotic diseases in domestic animals and wildlife, and the priority given by the World Health Organization (WHO) to the eradication of a number of diseases are all factors that underscore the importance of vaccines. Prior to the approval of new vaccines for use in humans and animals, regulatory authorities require demonstration of their safety and efficacy. To ensure that post-approval production of each lot of vaccine maintains the antigenic characteristics that make them effective, immunization or immunization-challenge procedures in laboratory animals are sometimes used. Animals may also be used for post-licensing safety testing to detect vaccine toxicity in order to prevent the release of lots that might cause serious adverse health effects. In recent years, efforts have increased to develop alternative methods that reduce, refine (less pain and distress), and replace the use of animals for vaccine potency and safety testing. This workshop will bring together an international group of scientific experts from government, industry, and academia to review the current state of the science, availability, and future need for alternative methods that can reduce, refine, and replace the use of animals for human and veterinary vaccine post-licensing potency and safety testing. Plenary and breakout sessions will address current U.S. and international regulatory requirements, currently available alternatives, and future research, development, and validation activities needed to further advance the use of alternative methods for vaccine post-licensing potency and safety testing.

Workshop Goals

1. Review the state of the science of alternative methods that are currently available and/or accepted for use that reduce, refine (less pain and distress), and replace the use of animals in vaccine potency and safety testing, and discuss ways to promote their implementation.
2. Identify knowledge and data gaps that must be addressed to develop alternative methods that can further reduce, refine, and replace the use of animals in vaccine potency and safety testing.
3. Identify and prioritize research, development, and validation efforts needed to address these knowledge and data gaps in order to advance alternative methods for vaccine potency and safety testing while ensuring continued protection of human and animal health.

Workshop Objectives

1. Review the public health needs and regulatory requirements for vaccine potency and safety testing.
2. Review currently available and/or accepted alternative methods that reduce, refine, and replace the use of animals for vaccine potency and safety testing.
3. Identify and discuss the current development and/or validation status of proposed alternative methods for vaccine potency and safety testing and their potential to reduce, refine, and replace current *in vivo* assays.
4. Identify knowledge and data gaps and identify and prioritize future research, development, and validation initiatives to address these gaps.
5. Discuss how to promote the collection and sharing of data in order to advance the development and validation of methods that reduce, refine, and replace the use of animals in vaccine potency and safety testing.
6. Discuss ways to promote international harmonization and/or acceptance of vaccine potency and safety requirements, including the acceptance of alternative methods that reduce, refine, and replace the use of animals in vaccine potency and safety testing.

Workshop Agenda

Day 1, Tuesday, September 14, 2010

7:30-8:30 Registration and Poster Setup

8:30-8:45 Opening Session: Welcoming Remarks and Overview of Workshop Objectives

Session 1
Overview of Public Health Needs and Regulatory Requirements for Vaccine Safety and Potency Testing

This session will summarize the public health needs, regulatory requirements and rationale in the U.S., Europe, and Asia, as well as in developing countries, to determine potency and efficacy of vaccine products.

8:50 History and Overview of Human Vaccines and their Importance to Public Health
Speaker pending, National Institute of Allergy and Infectious Diseases.

9:15 History and Overview of Veterinary Vaccines and their Importance to Animal Health
James Roth, D.V.M., Ph.D. College of Veterinary Medicine, Iowa State University.

9:40 U.S. FDA Requirements for Human Vaccine Safety and Potency Testing
Theresa Finn, Ph.D., Center for Biologics Evaluation and Research, U.S. FDA.

10:00 USDA Requirements for Veterinary Vaccine Safety and Potency Testing
Richard E. Hill Jr., D.V.M., Center for Veterinary Biologics, USDA.

10:20 Break

10:40 International Regulatory Requirements for Vaccine Safety and Potency Testing: Roundtable Discussion
Richard Isbrucker, Ph.D., Health Canada, Canada.
Ralph Woodland, Ph.D., Veterinary Medicines Directorate, United Kingdom.
Yoshinobu Horiuchi, Ph.D., Pharmaceuticals and Medical Devices Agency, Japan.
JinHo Shin, Ph.D., World Health Organization, Switzerland.

Session 2
Replacement Methods for Vaccine Potency Testing: Current State of the Science and Knowledge Gaps

This session will review currently accepted replacement alternatives that do not require the use of animals for vaccine potency testing (i.e., antigen quantification), knowledge gaps associated with test methods not currently accepted, and areas that should be emphasized as targets for future development. This session will summarize recent conclusions and recommendations from other relevant workshops and outline successes in replacing the use of animals for vaccine potency tests.

11:20 Overview of Currently Approved Veterinary Vaccine Potency Testing Methods and Methods in Development That Do Not Require Animal Use
Hans Draayer, M.Sc., Pfizer Animal Health

11:45 Case Study of Development, Validation, and Acceptance of a Non-animal Method for Assessing Veterinary Vaccine Potency
Ivo Claassen, Ph.D., Central Veterinary Institute, The Netherlands.

12:10 Lunch

1:10 Overview of Currently Approved Human Vaccine Potency Testing Methods That Do Not Require Animal Use
Willie F. Vann, Ph.D., Center for Biologics Evaluation and Research, U.S. FDA.

1:35 Overview of the Current Status of Human Vaccine Potency Testing Methods in Development That May Replace Animals
Robin Levis, Ph.D., Center for Biologics Evaluation and Research, U.S. FDA.

2:00 Case Study of Development, Validation, and Acceptance of a Non-Animal Method for Assessing Human Vaccine Potency
Johan Descamps, Ph.D., GlaxoSmithKline Biologicals, Belgium.

2:25 Break

2:45 Breakout Groups: Non-animal Replacement Methods for Vaccine Potency Testing: Current State-of-the-Science, Knowledge Gaps, and Research Needs

Group No. 1: Human Vaccines

Group No. 2: Veterinary Vaccines

5:00-6:00 Poster Session

Day 2, Wednesday, September 15, 2010

7:30-8:30 Registration

8:30 Breakout Group Reports and Discussion

Session 3
Animal Use for Vaccine Potency Testing: Refinement and Reduction Alternatives

This session will provide an overview of alternative methods and approaches that, if sufficiently validated, could (1) refine current vaccine potency testing procedures to reduce or eliminate animal pain and distress and/or (2) reduce the number of animals used for specific vaccine potency testing procedures.

Session 3A
Refinement Alternatives: Using Serological Methods to Avoid Challenge Testing

This topic will review current refinement alternatives to vaccine potency testing that do not require the challenge test. Speakers will also address subsequent reduction in animal use when using serological methods and how these were validated.

9:35 Refinement Alternatives for Human Vaccine Potency Testing: Overview of Currently Approved Serological Methods
James Keller, Ph.D., Center for Biologics Evaluation and Research, U.S. FDA.

10:00 Refinement Alternatives for Veterinary Vaccine Potency Testing: Overview of Currently Approved Serological Methods
Geetha Srinivas, D.V.M., Ph.D., Center for Veterinary Biologics, USDA.

10:25 Break

10:45 Animal Refinement and Reduction Alternative Approaches for Vaccine Potency Testing of Diphtheria and Tetanus Vaccines
Dorothea Sesardic, Ph.D., National Institute for Biological Standards and Control, United Kingdom.

11:10 Development and Validation of Serological Methods for Human Vaccine Potency Testing: Case Study of an Anthrax Vaccine
Juan Arciniega, D.Sc., Center for Biologics Evaluation and Research, U.S. FDA.

11:35 Development and Validation of Serological Methods for Veterinary Vaccine Potency Testing: Case Study of a Veterinary Vaccine
Jeffrey Galvin, Ph.D., Pfizer Animal Health

12:00 Lunch

Session 3B
Refinement Alternatives: Using Earlier Humane Endpoints to Avoid or Minimize Animal Pain and Distress in Vaccine Potency Challenge Testing

This session will address the currently accepted and required endpoints for vaccine potency challenge tests, for situations where accepted serological tests are not yet available. The status of earlier more humane endpoints that can or could be used as an alternative to death or moribund euthanasia from both human and veterinary perspectives will also be addressed.

1:00 Overview of Current Humane Endpoints in Human and Veterinary Vaccine Potency Testing
Coenraad Hendriksen, D.V.M., Ph.D., Netherlands Vaccine Institute, The Netherlands.

Session 3C
Reduction Alternatives: Strategies to Further Reduce Animal Numbers for Vaccine Potency Testing

This session will focus on methods and approaches that can be used to reduce the number of animals used in vaccine potency testing, while still attaining the testing objectives. Current methods and approaches in development that may further reduce animal use for vaccine potency testing will also be addressed.

1:25 Overview of Current Reduction Methods and Reduction Methods in Development for Vaccine Potency Testing
Geetha Srinivas, D.V.M., Ph.D., Center for Veterinary Biologics, USDA.

1:50 Application of the Consistency Approach for Reducing Animal Use in Vaccine Potency Testing
Jodie Kulpa-Eddy, D.V.M., Animal & Plant Health Inspection Service, USDA.

2:15 Break

2:35 Breakout Groups: Methods and Strategies for the Refinement and Reduction of Animal Use for Vaccine Potency Testing

Group No. 1: Human Vaccines

Group No. 2: Veterinary Vaccines

Day 3, Thursday, September 16, 2010

7:30-8:30 Registration

8:30 Breakout Group Reports and Discussion

Session 4
Vaccine Safety Testing: Post-licensing Reduction, Refinement and Replacement Methods and Strategies

This session will focus on current regulatory requirements and rationale for post-license vaccine safety testing (e.g., general safety test, neurovirulence test, pyrogen test) from both a human and animal perspective. This session does not include requirements for vaccine potency testing.

9:35 Human Vaccine Post-license Safety Testing: Overview of Current Regulatory Requirements and Accepted Alternatives
Theresa Finn, Ph.D., Center for Biologics Evaluation and Research, U.S. FDA.

10:00 Veterinary Vaccine Post-license Safety Testing: Overview of Current Regulatory Requirements and Accepted Alternatives
Glen Gifford, D.V.M., M.Sc., Canadian Food Inspection Agency, Canada.

10:25 Break

10:55 Target Alternative Vaccine Safety Testing Strategies for Pertussis Toxin
Juan Arciniega, D.Sc., Center for Biologics Evaluation and Research, U.S. FDA.

11:20 Current Research and Development Activities Directed Toward Replacement of the Neurovirulence Test in Vaccine Safety Testing
Steven Rubin, Ph.D., Center for Biologics Evaluation and Research, U.S. FDA.

11:45 Lunch

12:45 Breakout Groups: Post-license Vaccine Safety Testing: Alternative Strategies for the Replacement, Refinement, and Reduction of Animals

Group No. 1: Human Vaccines
Group No. 2: Veterinary Vaccines

3:00 Break

3:20 Breakout Group Report and Discussion

Group No. 1: Human Vaccines
Group No. 2: Veterinary Vaccines

4:20 Closing Comments

4:30 End of Meeting

Draft List of Vaccines Applicable to the Workshop:

- Tetanus
- Diphtheria
- Pertussis
- Cholera
- Rabies
- Leptospirosis
- Erysipelas
- Hepatitis A
- Hepatitis B
- Inactivated poliovirus
- Oral poliomyelitis
- Anthrax
- Combination Vaccines